FUNCTIONAL STUDY OF ATRIAL CONTRACTION IN A MURINE HEART MODEL

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Background

- Atrial Fibrillation (AF) is the most common cardiac arrhythmia in humans
- The high frequency and erratic contractions seen during AF makes the manual analysis of individual contraction curves impossible. Therefore, a highly sensitive analytical programme must be used

Objectives

In collaboration with "SNiP-FIB" this thesis collected contraction curve data obtained from stimulated isolated murine atria and compared the obtained results with existing literature in order to determine whether Xavier Mormon's analytical programme:

1. Was able to correctly analyse the contractile curve data obtained
2. Is an adequate tool for the analysis of contraction curves in AF models

Methods

Isolated murine atria were stimulated in an organ bath with varying frequencies of electrical pulses and increasing concentrations of carbachol followed by a unique dose of atropine (Diagram 1)

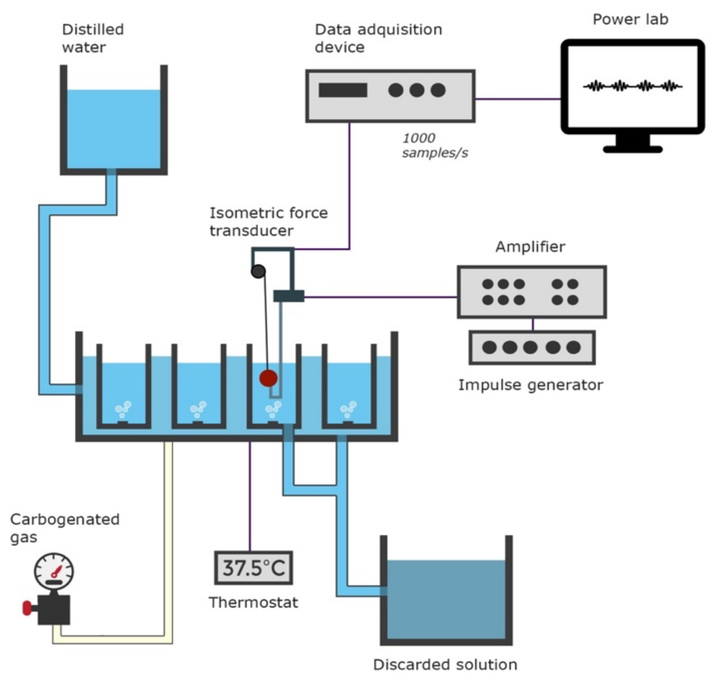
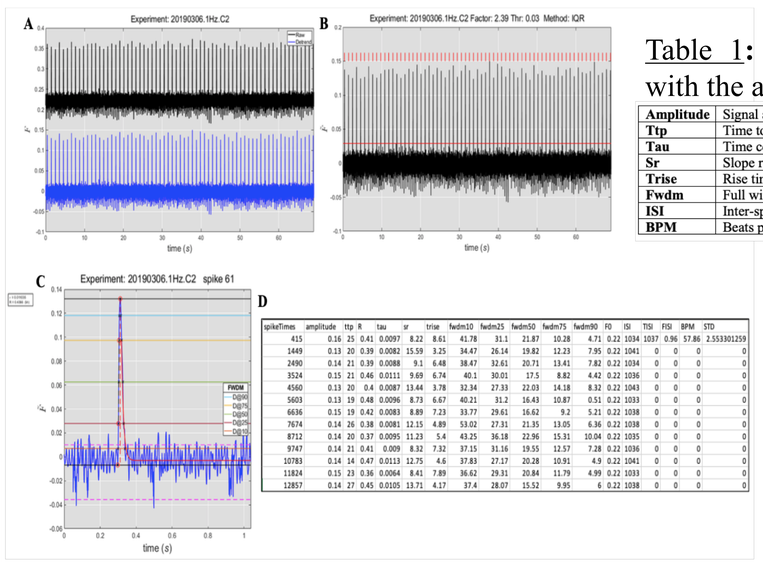


Diagram 1: Schematic representation of the automatic organ bath and isometric force transducer

The analytical programme isolated individual contraction curves from each stimulation protocol and the values for amplitude, Ttp, Tau, Sr, Trise, Fwdm, ISI, BPM and R^2 were calculated (Figure 1 and Table 1)



spikeTimes	amplitude	ttp	R	tau	sr	trise	fwdm10	fwdm25	fwdm50	fwdm75	fwdm90	F0	ISI	TISI	FISI	BPM	STD
415	0.16	25	0.41	0.0097	8.22	8.61	41.78	31.1	21.87	10.28	4.71	0.22	1034	1037	0.96	57.86	2.553301259
1449	0.13	20	0.39	0.0082	15.59	3.25	34.47	26.14	19.82	12.23	7.95	0.22	1041	0	0	0	0
2490	0.14	21	0.39	0.0088	9.1	6.48	38.47	32.61	20.71	13.41	7.82	0.22	1034	0	0	0	0
3524	0.15	21	0.46	0.0111	9.69	6.74	40.1	30.01	17.5	8.82	4.42	0.22	1036	0	0	0	0
4560	0.13	20	0.4	0.0087	13.44	3.78	32.34	27.33	22.03	14.18	8.32	0.22	1043	0	0	0	0
5603	0.13	19	0.48	0.0096	8.73	6.67	40.21	31.2	16.43	10.87	0.51	0.22	1033	0	0	0	0
6636	0.15	19	0.42	0.0083	8.89	7.23	33.77	29.61	16.62	9.2	5.21	0.22	1038	0	0	0	0
7674	0.14	26	0.38	0.0081	12.15	4.89	53.02	27.31	21.35	13.05	6.36	0.22	1038	0	0	0	0
8712	0.14	20	0.37	0.0095	11.23	5.4	43.25	36.18	22.96	15.31	10.04	0.22	1035	0	0	0	0
9747	0.14	21	0.41	0.009	8.32	7.32	37.15	31.16	19.55	12.57	7.28	0.22	1036	0	0	0	0
10783	0.14	14	0.47	0.0113	12.75	4.6	37.83	27.17	20.28	10.91	4.9	0.22	1041	0	0	0	0
11824	0.15	23	0.36	0.0064	8.41	7.89	36.62	29.31	20.84	11.79	4.99	0.22	1033	0	0	0	0
12857	0.14	27	0.45	0.0105	13.71	4.17	37.4	28.07	15.52	9.95	6	0.22	1038	0	0	0	0

Table 1: values (with units) calculated with the analytical program

Amplitude	Signal amplitude	g
Ttp	Time to peak	ms
Tau	Time constant (of fall)	adimensional
Sr	Slope rate (of rise)	g/ms
Trise	Rise time detected from 25% to 75% of reference levels	ms
Fwdm	Full width at reference levels (10%, 25%, 50%, 75% + 90%)	ms
ISI	Inter-spike interval	ms
BPM	Beats per minute	adimensional

Figure 1: A graphic representation of raw signal (1A), spike detection (1B), transient kinetics (1C) and the data obtained for each parameter (1D) from the analytical program for one stimulation protocol

Conclusions

The analytical programme used in this thesis is useful for the analysis of contraction curve parameters in isolated murine atria and could, therefore, be an appropriate tool for the study of atria with AF

Results

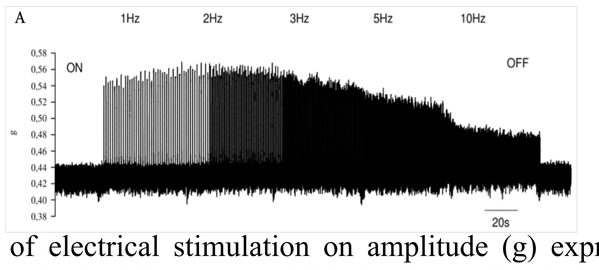


Figure 2: The effect of electrical stimulation on amplitude (g) expressed over time in one left atrium. This graph was obtained from *Powerlab* before normalization.

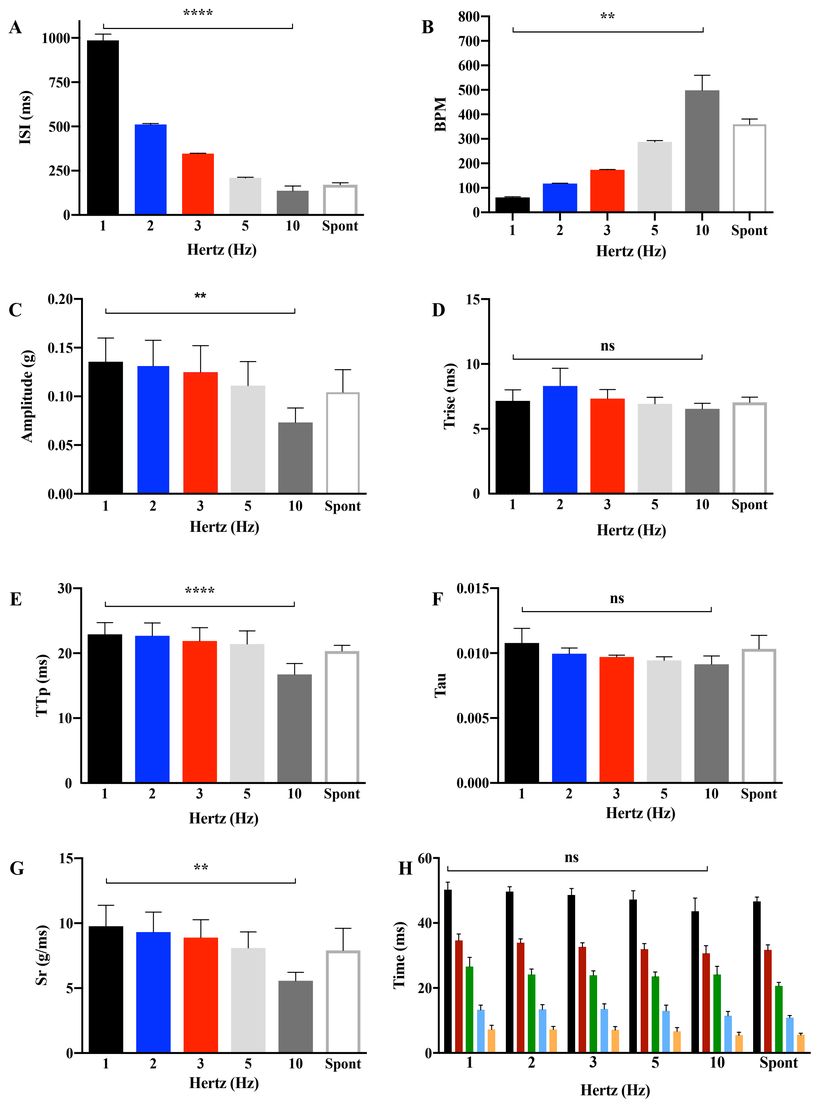


Figure 3: (A-H): The effect of 1, 2, 3, 5 and 10 Hz of electrical stimulation on ISI (ms), BPM, Amplitude (g), Trise (ms), TTp (ms), Tau, Sr (g/ms) and Fw (ms) in n=6 isolated left and right (spontaneous) murine atria (Median values ± SEM statistically analyzed with ANOVA paired t-tests).

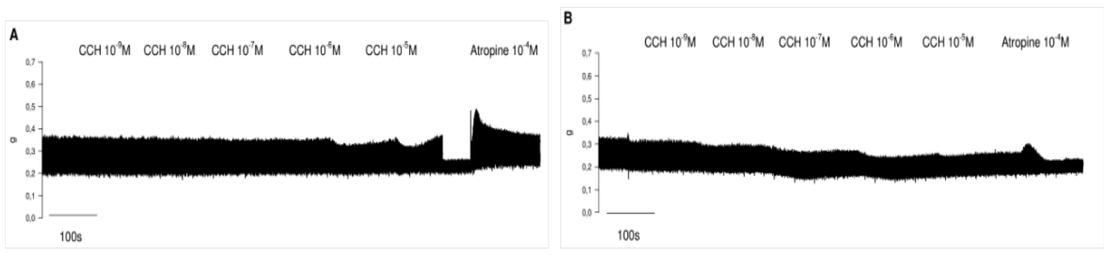


Figure 4 (A-B): The effect of ascending concentrations of carbachol and 10^{-4}M of atropine on the amplitude (g) of one right (A) and one left (B) isolated murine atria. These graphs were obtained from *Powerlab* before normalization.

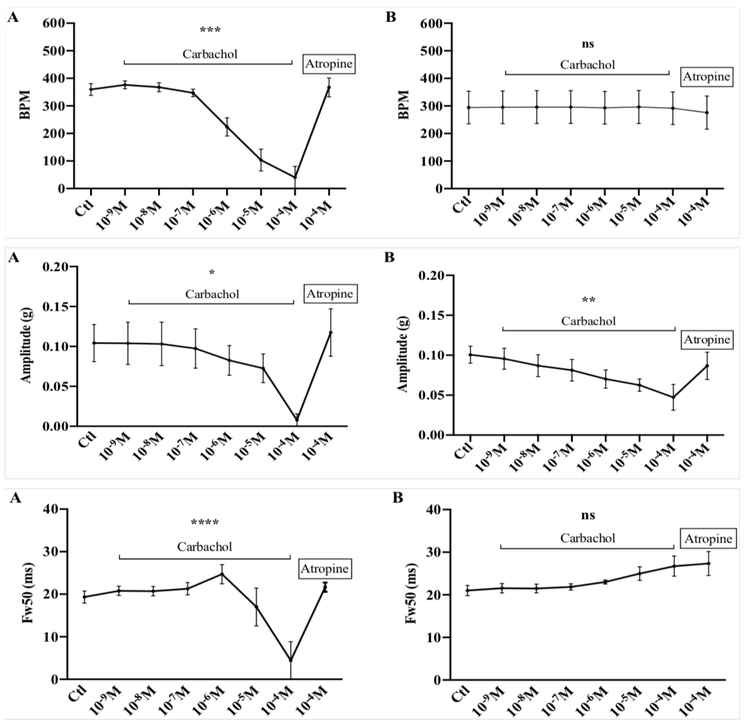


Figure 5: The effect of ascending concentrations of carbachol and 10^{-4}M of atropine on BPM, amplitude (g) and Fw50 (ms) in n=6 right (A) and n=5 left (B) isolated murine atria (Median values ± SEM statistically analyzed with ANOVA paired t-tests)